



## Glossary of Terms

**Acyl-Coenzyme A: Cholesterol Acyltransferase:** The gene for this enzyme is on chromosome 1. It is an enzyme located in the membrane of the endoplasmic reticulum (ER) and acts to join cholesterol molecules to long chain fatty acids for storage purposes.

**Acid Sphingomyelinase (ASM):** This is a lysosomal enzyme that breaks down a substance called Sphingomyelin. This enzyme is defective to a greater or lesser extent in NPA/B disease.

**Allele:** Particular form of gene. Alleles occur in pairs, one on each chromosome inherited from each parent.

**Amino Acids:** Organic molecules that link together to form proteins.

**Autosomal:** Refers to chromosomes 1 to 22; i.e. any chromosome other than the sex chromosomes.

**Bases:** In the context of this web site. Used to describe a number of chemicals that are used as instruction code by DNA and RNA. These are abbreviated A, T, C, G in DNA and A, U, C, G in RNA.

**Blood Brain Barrier:** A highly selective barrier formed by blood vessels and a type of brain cell called astrocytes that allow only appropriate molecules to cross from blood to brain; e.g. oxygen and sucrose. It aims to keep harmful molecules out of the brain.

**Calcium:** An essential element of all animals and plants. Vital in all cells.

**Catalysts:** A substance that accelerates a chemical reaction without being changed itself. Enzymes are a type of catalyst.

**Cells:** The basic unit for life, bound by a protective membrane. Cells contain all the information; lysosome, mitochondria, nucleus, DNA, production mechanisms, material and communication links with other cells to replicate and grow into a living creature which allow cells to replicate and function. (See diagram)

**Cerebellum:** Part of the brain located behind the brain stem under the main mass of the brain. Is known to be responsible for the co-ordination of movement and contains Purkinje cells which are badly affected in NPC.

**Cholesterol:** A fatty substance known as a sterol that is a major component of cell membranes, especially the main (plasma) membrane. It is also required for digestive bile acids and sterol hormones. Some cholesterol is taken in from certain foods but most is produced by the cells of the body, notably the liver. A constant supply of cholesterol is needed for cell growth and maintenance and is distributed in the blood stream by LDL.

**Cholesteryl Esterase:** A lysosomal enzyme that cuts (hydrolyses) LDL cholesterol molecules free from their fatty acid tails. Wolman's disease results from defects in this enzyme.

**Chromosomes:** Very long super-coiled DNA molecule that carries the information template enabling replication of cells and the associated living creature. Located in the cell's nucleus.

**Common mutation:** A mutation in a gene that occurs in a high percentage of patients affected by a specific disease. E.g. I1061T in NPC.

**Cytosol:** The internal liquid/gel content of a cell that surrounds the sub-cellular organelles and contains many of the simple and complex molecules required for the cell to function. The cytosol is not uniform but varies throughout its extent and is organized by the internal skeleton of the cell.

**Diploid:** Cells containing two sets of chromosomes and hence, two copies of genes. Most cells of an organism except sex cells and red blood cells are diploid.

**DNA:** De-oxy ribose nucleic acid. A very long molecule and the main component of chromosomes. DNA contains a code which, when processed by the cell's production machinery, produces proteins. It also contains information relating to the timing and life cycle of the cell.

**Dominant (allele):** Only one copy of the allele is needed to produce a certain characteristic. E.g. if you have one allele for brown eyes and one for blue, brown is dominant and you will have brown eyes.

**Endoplasmic reticulum:** series of interconnected flattened cavities lined with a thin membrane which is continuous with the nuclear membrane.

**Endosomes:** A membrane-bound compartment of the cell; the destination for internalized plasma membrane components and the internalization of external molecules.

**Enzyme:** A protein that acts as a catalyst accelerating chemical reaction.

**Esterification:** A type of chemical reaction carried out by an enzyme. In NPC it relates to the attaching of long chain fatty acids to cholesterol and renders the cholesterol molecule chemically inactive. A molecule of water is given off in this reaction. Reversing this process and separating cholesterol from the fatty acid is called hydrolysis.

**Fibroblasts:** Cells found in connective tissue associated with healing wounds. Skin fibroblasts often grown to be used extensively in laboratory testing.

**Filipin:** A blue substance used to stain fibroblast cells. Appears fluorescent under the microscope.

**Gametes:** Sex cells. Sperm cells and ova. These are haploid cells.

**Gangliosides:** A form of glycolipid. A component of cell membranes especially abundant in nerve cells. Found to be abnormal in NPC.

**Genes:** Regions of DNA that are copied to make proteins.

**Genome:** The total complement of genes on all the chromosomes that define a person or animal's life cycle.

**Genotype:** Genetic make-up of an individual

**Glycolipids:** A group of lipids containing a carbohydrate.

**Glycosphingolipids:** sphingolipids with one or more carbohydrate attached.

**Golgi apparatus:** Golgi- a membrane bound compartment of the cell, acts as a branch point between proteins destined for the lysosomes via the plasma membrane.

**HMGCoA Reductase:** An enzyme that operates within the cells own cholesterol manufacturing pathway. This pathway is known as the de novo pathway, or as new. This is a separate pathway to the LDL method of obtaining cholesterol.

**Haploid:** Cells that contain one set of chromosomes. These are the sex cells or gametes and red blood cells.

**Heterozygous:** A heterozygous condition exists if the corresponding genes on each of the related pair of chromosomes are different to each other. The different genes may be normal or disease causing.

**Homeostasis:** In the context of NPC, a state of balance of the cholesterol content of a cell. The supply of cholesterol has met the demanded amount and the cell has stopped importing via LDL and manufacturing.

**Homozygous:** A homozygous condition exists if the corresponding genes on each of the related pair of chromosomes are the same. The genes may both be normal or disease causing.

**LDL:** Low density lipoprotein. Manufactured in the liver and distributed to the other organs and cells of the body via the blood stream. The LDL particles contain esterified cholesterol within a membrane and also have a protein called Apo B100 which forms a strong bond with the LDL receptors on the surface of the cells. Too much LDL in the blood is considered to be a bad sign and an indicator of heart disease and stroke.

**LDL Receptor:** A receptor on the surface of a cell that binds LDL particles prior to transferring them to the interior of the cell. The receptor appears in abundance during cellular cholesterol demand and then diminishes to a low level once the demand has been satisfied.

**Lipid:** An organic molecule that is insoluble in water. This property is important for the formation of membranes (very high lipid content) which allow separation of different biologically active solutions.

**Lysosomes:** Membrane bound organelles within the cell whose task is to re-cycle biochemical molecules for re-use. They contain a variety of enzymes for this purpose.

**Meiosis:** A special type of cell division that produces sex cells (ova or sperm) each containing half or a haploid set of chromosomes.

**Metabolism:** All processes taking place in living cells. Main processes are anabolic – building up of complex molecules from simpler ones and, catabolic – the breaking down of complex molecules into simpler ones.

**Mitochondria:** Cellular organelles that produce much of the cells energy requirements. Mitochondria contain their own DNA which is inherited only through the female line.

**Mitosis:** A complex process of cell division whereby two cells are produced from one, each with its own complement of chromosomes, membranes, organelles and cytosol.

**Mutagen:** An agent that is capable of increasing mutation rate in an organism, e.g. excessive X-rays.

**Mutations:** Heritable changes in the DNA of cells. Often changes that could be detrimental to the operation of the cell.

**Neurodegenerative:** Causing loss of function of a system due to the loss of or damage to cells in the nervous system.

**Neuropathology:** The structure and function of the nervous system.

**Nucleus:** A membrane bound organelle within a cell that contains the chromosomes.

**Organelle:** A sub unit of the cell usually bound by a membrane and distinct in its composition and functional behavior. Examples include: - the nucleus, endoplasmic reticulum, Golgi apparatus, mitochondria, lysosomes, and endosomes.

**Ova:** Plural of ovum, the female sex cell or egg. A haploid cell.

**Plasma membrane:** (cell membrane) The outer boundary of cells.

**Polymorphisms:** Variations of genes (DNA) that may improve, degrade or leave unchanged, the capability of the associated protein. They contribute towards the differences between individuals in a population.

**Proteins:** Large organic molecules that perform many of the metabolic activities taking place within a cell. Typical roles are as enzymes, transporters, communications, sensors, activators and structural elements. The proteins are constructed from chains of amino acids linked together in a sequence defined by the DNA of genes.

**Purkinje Cells:** Large neurons of the cerebellum where they form a single layer. They are thought to be the only cells of the cerebellum with outgoing connections to the rest of the brain. These cells are vulnerable to damage and death in NPC.

**RNA:** Ribonucleic Acid. A chemical found in the nucleus and cytoplasm of cells; it plays an important role in the formation of proteins and other chemical activities of the cell. The structure of RNA is similar to that of DNA.

**Recessive:** The effects of a gene that are masked by the activity of the same gene on the other chromosome (see dominant).

**Ribosomes:** Small cellular components composed of specialized ribosomal RNA and protein, site of protein synthesis.

**Sex- chromosomes:** non autosomal chromosomes- X and Y inherited from parents. XX is female, XY is male.

**Sex-Linked:** Traits that may be either normal or disease causing that are derived from the genes or DNA of the X, Y chromosomes or mitochondrion (as opposed to autosomal).

**Sperm:** A male sex cell or gamete containing a haploid (one) set of chromosomes.

**Sphingolipids:** A type of molecule found in all plant and animal cells. They are particularly abundant in the tissues of the nervous system.

**Sphingomyelin:** A complex organic molecule that is present in membranes in association with cholesterol. Especially found in neurons and is not processed correctly in NPA/B.

**Steroids:** A type of lipid e.g. Cholesterol, bile acids, some vitamins (including Vit D) and steroid hormones.

**Substrate:** A substance on which an enzyme acts to form either a more complex substance or a simpler substance.

**Transcribe:** In terms of the cell, the process of turning the information contained on a RNA template into a protein. This task is conducted by organelles called ribosomes.

**Translate:** the process of using RNA to produce a protein.

**X-linked:** Traits associated with the X chromosome which may be normal or disease causing.

**Zygote:** A fertilized ovum. Two haploid cells, sperm and ovum, combining to form a diploid cell.

